REMARKS

The foregoing amendment to the specification is supported in Figure 2A as originally filed and does not introduce new matter.

The amendment to Figure 2A merely adds a sequence identifier to the figure to comply with 37 C.F.R. 1.821(d) and does not introduce new matter.

Enclosed is a marked-up version of the changes made by this amendment. The enclosed pages are captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE**"

Entry of the foregoing amendment is respectfully requested and favorable action on the merits is earnestly solicited.

Date: December 4, 2002

Respectfully submitted,

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CERTIFICATE OF MAILING UNDER 37 CFR 1.8

I hereby certify that this correspondence and its listed enclosures is being deposited with the United States Postal Service as First Class Mail, postage paid, in an envelope addressed to: Commissioner for Patents, Washington, D.C. 20231on **December 4, 2002**

Name: **Deborah A. Mojarro**

Signed: _____ Date: 12/4/02

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Page 8, lines 12-15 have been amended as follows:

Figure 2A-2B shows design of the targeting construct used to disrupt nuclear hormone receptor genes. Figure 2A, which illustrates the target sequence (SEQ ID NO:1) for the targeting construct, shows the location and extent of the disrupted portion of the nuclear hormone receptor gene, as well as the nucleotide sequences flanking the Neo' insert in the targeting construct. Figure 2B shows the sequences identified as SEQ ID NO:3 and SEQ ID NO:4, which were used as the targeting arms (homologous sequences) in the nuclear hormone receptor targeting construct.

Construct

GI Number(s): 2267577

Gene Family: Nuclear Hormone Receptor

Gene Subfamily: Orphan NHR

Gene Sequence: full-length cDNA, Mouse

underlined = deleted in targeting construct

[ ] = sequence flanking Neo insert in targeting construct

CCCTCGACCTCGAGATCCATTGTGCTCTAAAGCAGAGTCTGGGTCCTACCTACATATGGC
ACCGAGGATACCTAGAGGCCCCATGCAAGAGAAGGCCCTTGTTTTCCAGGCACTGAGGAC
CGCAGTCCCTAATTCCTGGCACTTCCTGAGATCTCAAGGAAAGCAGGGTCAGCGAGGAGG
CCTGGGGAGAGGAGGCATCCTACACCCAATCTTGTGGCCTCCTCCCTAAGGGAAACAG[GA
GACCATGACAGCTATGCTAACACTAGAAACCATGGCCAGTG]AAGAAGAATATGGGCCGAG
GAACTGTGTGGTGTGTGGAGACCGGGCCACAGGCTATCATTTCCACGCCCTGACTTGTGA
GGGCTGCAAGGGCTTCTTCAGACGAACAGTCAGCAAAACCATT[GGTCCCATCTGTCCGTT
TGCTGGAAGGTGTGAGGTCAGCAAGGCCCAGAGACGCCACTGTCCAGCCTGCAGGTTGCA
GAAGTGTCTAAATGTTGGCATGAGGAAAGACA]TGATACTGTCAGCAGAAGCCCTGGCATT
GTGGTGAGCCAGACAGGCACAGCGGCGGGCAGACAAAGCATCTTTGCAACTGAATCAGCA
GCAGAAAGAACTGGTCCAGATCCTCCTGGGGGCCCACACTCGCCATGTGGGCCCATTGTT
TGACCAGTTTGTGCAGTTCAAGCCTCCAGCCTATCTGTTCATGCATCACCGGCCTTTCCA
GCCTCGGGGCCCCGTGTTGCCTCTGCTCACACACTTTGCAGATATCAACACGTTTATGGT
GCAACAGATCATCAAGTTCACCAAGGATCTGCCGCTCTTCCGGTCCCTAACCATGGAGGA
CCAGATCTCCCTTCTCAAGGGAGCGGCTGTGGAAATATTGCATATCTCACTCAACACTAC
CTTCTGTCTTCAAACAGAGAATTTCTTCTGTGGGCCTCTTTGCTACAAGATGGAGGACGC
AGTCCATGCAGGGTTCCAGTACGAGTTTTTGGAGTCGATCCTCCACTTCCATAAAAACCT
GAAAGGACTGCATCTCCAGGAGCCTGAGTATGTGCTCATGGCTGCCACGGCCCTCTTCTC
CCCTGGTTTCTGTATGCAAAGCTGATGGGCCTGCTGGCTGACCTCCGGAGTATAAACAAT
GCATACTCCTATGAACTTCAGCGCTTGGAGGAACTGTCTGCTATGACGCCGCTGCTCGGG
GAGATTTGCAGTTGAGGCCCAGGCTTGCATCCTTTCCCCAGACCCCCAGGGATACACTGG
CCTGGAAAGGGTACAGCGCTGGACCCCACACAGCAGAAGGAGCTTGGGAGTGGCAATGAA
ATGCTGAACAGT

Gene Sequence Structure *

282 bp | Sequence Deleted | 403 bp

Size of full-length cDNA: 1332 bp

FIG. 2A

Construct

GI Number(s): 2267577

Gene Family: Nuclear Hormone Receptor

Gene Subfamily: Orphan NHR

Gene Sequence: full-length cDNA, Mouse

underlined = deleted in targeting construct

[ ] = sequence flanking Neo insert in targeting construct

CCCTCGACCTCGAGATCCATTGTGCTCTAAAGCAGAGTCTGGGTCCTACCTACATATGGC
ACCGAGGATACCTAGAGGCCCCATGCAAGAGAAGGCCCTTGTTTTCCAGGCACTGAGGAC
CGCAGTCCCTAATTCCTGGCAGTTCCTGAGATCTCAAGGAAAGCAGGGTCAGCGAGGAGG
CCTGGGGAGAGGAGGCATCCTACACCCAATCTTGTGGCCTGCTGCCTAAGGGAAACAGGA
[illegible]AAGAAGAATATGGGCGAG
GAACTGTGTGGTGTGTGGAGACCGGGCCACAGGCTATCATTTCCACGCCCTGACTTGTGA
GGGCTGCAAGGGCTTCTTCAGACGAACAGTCAGCAAAACCATTGGTCCCATCTGTCCGTT
TGCTGGAAGGTGTGAGGTCAGCAAGGCCCAGAGACGCCACTGTCCAGCCTGCAGGTTGCA
GAAGTGTCTAAATGTTGGCATGAGGAAAGACATGATACTGTCAGCAGAAGCCCTGGCATT
GCGGCGAGCCAGACAGGCACAGCGGCGGGCAGAGAAAGCATCTTTGCAACTGAATCAGCA
GCAGAAAGAACTGGTCCAGATCCTCCTGGGGGCCCACACTCGCCATGTGGGCCCATTGTT
TGACCAGTTTGTGCAGTTCAAGCCTCCAGCCTATCTGTTCATGCATCACCGGCCTTTCCA
GCCTCGGGGCCCCGTGTTGCCTCTGCTCACACACTTTGCAGATATCAACACGTTTATGGT
GCAACAGATCATCAAGTTCACCAAGGATCTGCCGCTCTTCCGGTCCCTAACCATGGAGGA
CCAGATCTCCCTTCTCAAGGGAGCGGCTGTGGAAATATTGCATATCTCACTCAACACTAC
GTTCTGTCTTCAAACAGAGAATTTCTTCTGTGGGCCTCTTTGCTACAAGATGGAGGACGC
AGTCCATGCAGGGTTCCAGTACGAGTTTTTGGAGTCGATCCTCCACTTCCATAAAAACCT
GAAAGGACTGCATCTCCAGGAGCCTGAGTATGTGCTCATGGCTGCCACGGCCCTCTTCTC
CCCTGGTTTCTGTATGCAAAGCTGATGGGCCTGCTGGCTGACCTCCGGAGTATAAACAAT
GCATACTCCTATGAACTTCAGCGCTTGGAGGAACTGTCTGCTATGACGCCGCTGCTCGGG
GAGATTTGCAGTTGAGGCCCAGGCTTGCATCCTTTCCCCAGACCCCCAGGGATACACTGG
CCTGGAAAGGGTACAGCGCTGGACCCCACACAGCAGAAGGAGCTTGGGAGTGGCAATGAA
ATGCTGAACAGT (SEQ ID NO:1)

Gene Sequence Structure *

282 bp — **Sequence Deleted** — 403 bp

Size of full-length cDNA: 1332 bp

FIG. 2A